

What is claimed is:

1. A method for detection and diagnosis of cancer comprising:  
detecting at least one biomarkers in a subject sample, and; correlating the detection of one or more protein biomarkers with a diagnosis of cancer, wherein the correlation takes into account the detection of one or more biomarker in each diagnosis, as compared to normal subjects

wherein the one or more protein markers are selected from:

- Marker I: having a molecular weight of about 8.6 kD
- Marker II: having a molecular weight of about 9.2 kD
- Marker III: having a molecular weight of about 19.8 kD
- Marker IV: having a molecular weight of about 39.8 kD
- Marker V: having a molecular weight of about 54 kD
- Marker VI: having a molecular weight of about 60 kD
- Marker VII: having a molecular weight of about 79 kD.

2. The method of claim 1 wherein one or more protein biomarkers are used to diagnose cancer.

3. A method for detection and diagnosis of ovarian cancer comprising:  
detecting at least one protein biomarkers in a subject sample, wherein the protein markers are selected from:

- Marker I: having a molecular weight of about 8.6 kD
- Marker II: having a molecular weight of about 9.2 kD
- Marker III: having a molecular weight of about 19.8 kD
- Marker IV: having a molecular weight of about 39.8 kD
- Marker V: having a molecular weight of about 54 kD
- Marker VI: having a molecular weight of about 60 kD
- Marker VII: having a molecular weight of about 79 kD

and; correlating the detection of one or more protein biomarkers with a diagnosis of ovarian cancer.

4. The method of claim 3 wherein one or more protein biomarkers are used to diagnose ovarian cancer.

5. The method of any one of claims 1 through 4 wherein a plurality of the biomarkers are detected.
6. The method of any one of claims 1 through 4 wherein at least two of the biomarkers are detected.
7. The method of any one of claims 1 through 4 wherein at least three of the biomarkers are detected.
8. The method of any one of claims 1 through 4 wherein at least four of the biomarkers are detected.
9. The method of any one of claims 1 through 4 wherein a single biomarker is used in combination with one or more known cancer biomarkers for diagnosing cancer.
10. The method of any one of claims 1 through 4 wherein a plurality of the markers are used in combination with one or more known cancer markers for diagnosing cancer.
11. The method of claim 9 or 10 wherein the known cancer markers are ovarian cancer markers for diagnosing ovarian cancer.
12. The method of 11 wherein the known ovarian cancer marker is CA 125.
13. The method of any one of claims 1 through 12 wherein the sample is selected from the group consisting of blood, blood plasma, serum, urine, tissue, cells, organs and vaginal fluids.
14. The method of any one of claims 1 through 13 wherein one or more protein biomarkers are detected by comparing protein profiles from patients susceptible to, or suffering from cancer with normal subjects.

15. The method of any one of claims 3 through 13 wherein one or more protein biomarkers are detected by comparing protein profiles from patients susceptible to, or suffering from ovarian cancer with normal subjects.
16. The method of any one of claims 1 through 15 wherein one or more protein biomarkers are detected using a biochip array.
17. The method of claim 16 wherein the biochip array is a protein chip array.
18. The method of claim 16 wherein the biochip array is a nucleic acid array.
19. The method of any one of claims 16 through 18 wherein the one or more markers are immobilized on the biochip array.
20. The method of claim 19 wherein immobilized one or more markers are subjected to laser ionization to detect the molecular weight of the markers.
21. The method of claim 20 wherein the molecular weight of the one or more markers is analyzed against a threshold intensity that is normalized against total ion current.
22. The method of claim 21 wherein logarithmic transformation is used for reducing peak intensity ranges to limit the number of markers detected.
23. The method of any one of claims 16 through 22 comprising:
  - generating data on immobilized subject samples on a biochip array, by subjecting said biochip array to laser ionization and detecting intensity of signal for mass/charge ratio; and,
  - transforming the data into computer readable form;
  - and executing an algorithm that classifies the data according to user input parameters, for detecting signals that represent markers present in ovarian cancer patients and are lacking in non-cancer subject controls.

24. The method of any one of claims 16 through 23 wherein the surface of the biochip array is hydrophobic.

25. The method of any one of claims 16 through 23 wherein the surface of the biochip array is ionic.

26. The method of claim 16 through 23 wherein the surface of biochip array is anionic.

27. The method of any one of claims 16 through 26 wherein the surface of the biochip array is comprised of immobilized nickel ions.

28. The method of any one of claims 16 through 23 wherein the surface of the biochip array is comprised of a mixture of positive and negative ions.

29. The method of any one of claims 16 through 28 wherein the surface of the biochip array comprises one or more antibodies.

30. The method of claim 16 through 29 wherein the surface of the biochip array comprises single or double stranded nucleic acids.

31. The method of any one of claims 16 through 29 wherein the surface of the biochip array comprises proteins, peptides or fragments thereof.

32. The method of any one of claims 16 through 29 wherein the surface of the biochip array comprises amino acid probes.

33. The method of any one of claims 16 through 29 wherein the surface of the biochip array comprises phage display libraries.

34. The method of any one of claims 1 through 33 wherein one or more of the markers are detected using laser desorption/ionization mass spectrometry, comprising:

providing a probe adapted for use with a mass spectrometer comprising an adsorbent attached thereto, and;  
contacting the subject sample with the adsorbent, and;  
desorbing and ionizing the marker or markers from the probe and detecting the deionized/ionized markers with the mass spectrometer.

35. The method of claim 34 wherein laser desorption/ionization mass spectrometry comprises:

providing a substrate comprising an adsorbent attached thereto;  
contacting the subject sample with the adsorbent;  
placing the substrate on a probe adapted for use with a mass spectrometer comprising an adsorbent attached thereto; and,  
desorbing and ionizing the marker or markers from the probe and detecting the desorbed/ionized marker or markers with the mass spectrometer.

36. The method of claim 35 wherein the adsorbent is hydrophobic, hydrophilic, ionic or metal chelate adsorbent.

37. The method of claim 35 wherein the adsorbent is comprised of nickel.

38. The method of claim 35 wherein the adsorbent is an antibody, single- or double stranded oligonucleotide, amino acid, protein, peptide or fragments thereof.

39. The method of any one of claims 1 through 33 wherein at least one or more protein biomarkers are detected using immunoassays.

40. A process for purification of a biomarker, comprising fractionating a sample comprising one or more protein biomarkers by size-exclusion chromatography and collecting a fraction that includes the one or more biomarker; and/or fractionating a sample comprising the one or more biomarkers by anion exchange chromatography and collecting a fraction that includes the one or more biomarkers.

41. The process of claim 40 wherein fractionation is monitored for purity on normal phase and immobilized nickel arrays.
42. The process of claim 41 for generating data on immobilized marker fractions on an array, comprising:
- subjecting said array to laser ionization and detecting intensity of signal for mass/charge ratio; and,
  - transforming the data into computer readable form;
  - and executing an algorithm that classifies the data according to user input parameters, for detecting signals that represent markers present in cancer patients and are lacking in non-cancer subject controls.
43. The process of claim 40 wherein fractions are subjected to gel electrophoresis and correlated with data generated by mass spectrometry.
44. The process of claim 43 wherein gel bands representative of potential markers are excised and subjected to enzymatic treatment.
45. The process of claim 44 wherein the enzyme treated gel bands are applied to biochip arrays for peptide mapping.
46. The process of any one of claims 40 through 45 wherein the one or more biomarkers are selected from:
- Marker I: having a molecular weight of about 8.6 kD
  - Marker II: having a molecular weight of about 9.2 kD
  - Marker III: having a molecular weight of about 19.8 kD
  - Marker IV: having a molecular weight of about 39.8 kD
  - Marker V: having a molecular weight of about 54 kD
  - Marker VI: having a molecular weight of about 60 kD
  - Marker VII: having a molecular weight of about 79 kD
47. A kit for aiding the diagnosis of cancer, comprising:

an adsorbent attached to a substrate, wherein the adsorbent retains one or more biomarker selected from:

- Marker I: having a molecular weight of about 8.6 kD;
- Marker II: having a molecular weight of about 9.2 kD;
- Marker III: having a molecular weight of about 19.8 kD;
- Marker IV: having a molecular weight of about 39.8 kD;
- Marker V: having a molecular weight of about 54 kD;
- Marker VI: having a molecular weight of about 60 kD; and
- Marker VII: having a molecular weight of about 79 kD.

48. The kit of claim 47 further comprising written instructions for use of the kit for detection of cancer.

49. The kit of claim 48 wherein the instructions provide for contacting a test sample with the absorbent and detecting one or more biomarkers retained by the absorbent.

50. The kit of any one of claims 47 through 48 wherein the substrate allows for adsorption of said adsorbent.

51. The kit of any one of claims 47 through 50 wherein the substrate can be hydrophobic, hydrophilic, charged, polar, metal ions.

52. The kit of any one of claims 47 through 51 wherein the adsorbent is an antibody, single or double stranded oligonucleotide, amino acid, protein, peptide or fragments thereof.

53. The kit of claim 47 or 48 wherein one or more protein biomarkers is detected using mass spectrometry.

54. The kit of claim 47 or 48 wherein one or more protein biomarkers is detected using immunoassays.

55. The kit of claim 54 wherein the immunoassay is an ELISA.

56. A method for diagnosing ovarian cancer comprising:  
detecting at least one biomarker from a subject sample, wherein the protein biomarker is selected from:

- Marker II: having a molecular weight of about 9.2 kD
- Marker III: having a molecular weight of about 19.8 kD
- Marker VI: having a molecular weight of 60 kD
- Marker VII: having a molecular weight of about 79 kD,

and; correlating the detection of at least one protein biomarker with a diagnosis of ovarian cancer, wherein the correlation takes into account the detection of at least one or more protein biomarkers in each diagnosis, as compared to normal subjects.

57. The method of claim 56 wherein a single biomarker is used in combination with known ovarian cancer markers for diagnosing ovarian cancer.

58. The method of claim 56 wherein a plurality of the markers are used in combination with known ovarian cancer markers for diagnosing ovarian cancer.

59. The method of claim 57 or 58 wherein the known ovarian cancer marker is CA 125.

60. The method of claim any one of claims 1 through 38 and 56 through 59 further comprising measuring the amount of each biomarker in the subject sample and determining the ratio of the amounts between the markers.

61. The method of any one of claims 1 through 38 and 56 through 60 further comprising measuring the amount of each biomarker in the subject sample and determining the ratio of the amounts between the biomarkers and known ovarian cancer markers.

62. The method of any one of claims 1 through 39 and 57 through 61 wherein the stage of ovarian cancer is assessed.

63. A purified protein selected from:

- Marker I: having a molecular weight of about 8.6 kD;



- Marker II: having a molecular weight of about 9.2 kD;
- Marker III: having a molecular weight of about 19.8 kD;
- Marker IV: having a molecular weight of about 39.8 kD;
- Marker V: having a molecular weight of about 54 kD;
- Marker VI: having a molecular weight of about 60 kD; and
- Marker VII: having a molecular weight of about 79 kD.

64. A composition comprising Marker I and one more biomarkers selected from Markers II, III, IV, V, VI, and VII.

65. A composition comprising Marker II and one more biomarkers selected from Markers I, III, IV, V, VI, and VII.

66. A composition comprising Marker III and at least one more biomarkers selected from Markers I, II, IV, V, VI, and VII.

67. A composition comprising Marker IV and at least one more biomarkers selected from Markers I, II, III, V, VI, and VII.

68. A composition comprising Marker V and at least one more biomarkers selected from Markers I, II, III, IV, VI, and VII.

69. A composition comprising Marker VI and one more biomarkers selected from Markers I, II, III, IV, V, and VII.

70. A composition comprising Marker VII and one more biomarkers selected from Markers I, II, III, IV, V, and VI.

71. A composition of any one of claims 65 through 70 wherein each of the markers are purified.

72. A method for qualifying ovarian cancer status in a subject comprising:

(a) measuring at least one biomarker in a sample from the subject, wherein the biomarker is selected from the group consisting of:

- Marker I: having a molecular weight of about 8.6 kD
- Marker II: having a molecular weight of about 9.2 kD
- Marker III: having a molecular weight of about 19.8 kD
- Marker IV: having a molecular weight of about 39.8 kD
- Marker V: having a molecular weight of about 54 kD
- Marker VI: having a molecular weight of about 60 kD
- Marker VII: having a molecular weight of about 79 kD, and

combinations of such Markers I through VII; and

(b) correlating the measurement with ovarian cancer status.

73. The method of claim 72 wherein a plurality of the biomarkers are measured.

74. The method of claim 72 wherein at least two of the biomarkers are measured.

75. The method of claim 72 wherein at least three of the biomarkers are measured.

76. The method of claim 72 wherein at least four of the biomarkers are measured.

77. The method of any one of claims 72 through 76 wherein one or more of the biomarkers are used in combination with one or more known cancer biomarkers for diagnosing cancer.

78. The method of 77 wherein the known ovarian cancer biomarker is CA 125.

79. The method of any one of claims 72 through 78 wherein the sample is selected from the group consisting of blood, blood plasma, serum, urine, tissue, cells, organs and vaginal fluids.

80. The method of any one of claims 72 through 79 wherein one or more biomarkers are detected by comparing protein profiles from patients susceptible to, or suffering from ovarian cancer with normal subjects.